Mary

Access DB# 65586

# SEARCH REQUEST FORM

**Scientific and Technical Information Center**

Requester's Full Name: P. Spivack Examiner #: 70400 Date: 4/29/02
Art Unit: 1614 Phone Number 30 84703 Serial Number: 09/978,132
Mail Box and Bldg/Room Location: 2D05 Results Format Preferred (circle): PAPER DISK E-MAIL
2D01

**If more than one search is submitted, please prioritize searches in order of need.** mej

**********

Please provide a detailed statement of the search topic, and describe as specifically as possible the subject matter to be searched. Include the elected species or structures, keywords, synonyms, acronyms, and registry numbers, and combine with the concept or utility of the invention. Define any terms that may have a special meaning. Give examples or relevant citations, authors, etc, if known. Please attach a copy of the cover sheet, pertinent claims, and abstract.

Title of Invention: Steven Curtis Zicker

Inventors (please provide full names): Karen J. Wedekind

Earliest Priority Filing Date: 10/31/2000

***For Sequence Searches Only* Please include all pertinent information (parent, child, divisional, or issued patent numbers) along with the appropriate serial number.**

Please search: methods for decreasing mental deterioration or increasing mental capacity comprising administering an antioxidant (such as lipoic acid or vitamin C [ascorbic acid] or vitamin E or l-carnitine) in a cat (feline) or a dog (canine) diet.

neur? degenerat? neurodegenerative disorder dementia cognit?

1539

Mary Hale – Supervisor, Info. Branch
STIC – Biotech/Chem. Library
CM-1 Room E01
703-308-4258

RECEIVED APR 29 2002 (STIC)

12.26
124.12
1364 2

thanks

**********

**STAFF USE ONLY**

Searcher: Mary
Searcher Phone #:
Searcher Location:
Date Searcher Picked Up:
Date Completed: 5/2
Searcher Prep & Review Time:
Clerical Prep Time:
Online Time: 9

**Type of Search**

NA Sequence (#)
AA Sequence (#)
Structure (#) ✓
Bibliographic
Litigation
Fulltext
Patent Family
Other

**Vendors and cost where applicable**

STN ~~124.12~~ 1364 2
Dialog
Questel/Orbit
Dr.Link
Lexis/Nexis
Sequence Systems
WWW/Internet
Other (specify)

PTO-1590 (8-01)

=> fil reg

| COST IN U.S. DOLLARS | SINCE FILE ENTRY | TOTAL SESSION |
|---|---|---|
| FULL ESTIMATED COST | 12.26 | 257.91 |

| DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS) | SINCE FILE ENTRY | TOTAL SESSION |
|---|---|---|
| CA SUBSCRIBER PRICE | 0.00 | -1.24 |

Dpuleck
978132

FILE 'REGISTRY' ENTERED AT 15:30:15 ON 02 MAY 2002


STRUCTURE FILE UPDATES: 30 APR 2002 HIGHEST RN 409303-45-3
DICTIONARY FILE UPDATES: 30 APR 2002 HIGHEST RN 409303-45-3

TSCA INFORMATION NOW CURRENT THROUGH July 7, 2001

Please note that search-term pricing does apply when conducting SmartSELECT searches.

Crossover limits have been increased. See HELP CROSSOVER for details.

Calculated physical property data is now available. See HELP PROPERTIES

Searched by: Mary Hale 308-4258 CM-1 12D16

for more information. See STNote 27, Searching Properties in the CAS Registry File, for complete details:
http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf

```
=> s (lipoic acid or vitamin c or ascorbic acid or vitamin e or "l-carnitine")/cn
             2 LIPOIC ACID/CN
             1 VITAMIN C/CN
             2 ASCORBIC ACID/CN
             1 VITAMIN E/CN
             1 "L-CARNITINE"/CN
L1           6 (LIPOIC ACID OR VITAMIN C OR ASCORBIC ACID OR VITAMIN E OR "L-CA
               RNITINE")/CN

=> fil medl,caplus,biosis,embase,jicst,wpids
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                      ENTRY    SESSION
FULL ESTIMATED COST                                   20.38     278.29

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)          SINCE FILE      TOTAL
                                                      ENTRY    SESSION
CA SUBSCRIBER PRICE                                    0.00      -1.24

FILE 'MEDLINE' ENTERED AT 15:30:56 ON 02 MAY 2002

FILE 'CAPLUS' ENTERED AT 15:30:56 ON 02 MAY 2002
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2002 AMERICAN CHEMICAL SOCIETY (ACS)

FILE 'BIOSIS' ENTERED AT 15:30:56 ON 02 MAY 2002
COPYRIGHT (C) 2002 BIOLOGICAL ABSTRACTS INC.(R)

FILE 'EMBASE' ENTERED AT 15:30:56 ON 02 MAY 2002
COPYRIGHT (C) 2002 Elsevier Science B.V.  All rights reserved.

FILE 'JICST-EPLUS' ENTERED AT 15:30:56 ON 02 MAY 2002
COPYRIGHT (C) 2002 Japan Science and Technology Corporation (JST)

FILE 'WPIDS' ENTERED AT 15:30:56 ON 02 MAY 2002
COPYRIGHT (C) 2002 THOMSON DERWENT

=> s (lipoic acid or vitamin c or ascorbic acid or vitamin e or "l-carnitine" or
l1)
L2         50638 FILE MEDLINE
L3        111575 FILE CAPLUS
L4         54288 FILE BIOSIS
L5         48534 FILE EMBASE
L6          7201 FILE JICST-EPLUS
L7         13100 FILE WPIDS

TOTAL FOR ALL FILES
L8        285336 (LIPOIC ACID OR VITAMIN C OR ASCORBIC ACID OR VITAMIN E OR "L-CA
                 RNITINE" OR L1)

=> s l8 and ((mental or neur?)(5a)(degenerat? or deteriorat? or capacit?) or
neurodegenerat?  or dementia)
L9           389 FILE MEDLINE
L10          319 FILE CAPLUS
L11          329 FILE BIOSIS
L12          628 FILE EMBASE
L13           43 FILE JICST-EPLUS
L14          102 FILE WPIDS


Searched by: Mary Hale 308-4258 CM-1 12D16
```

TOTAL FOR ALL FILES
L15 1810 L8 AND ((MENTAL OR NEUR?)(5A)(DEGENERAT? OR DETERIORAT? OR CAPAC IT?) OR NEURODEGENERAT? OR DEMENTIA)

=> s (antioxida? or anti oxid?) and ((mental? or neur?)(5a)(degenerat? or deteriorat? or capacit?) or neurodegenerat? or dementia)
L16 799 FILE MEDLINE
L17 815 FILE CAPLUS
L18 796 FILE BIOSIS
L19 828 FILE EMBASE
L20 51 FILE JICST-EPLUS
L21 173 FILE WPIDS

TOTAL FOR ALL FILES
L22 3462 (ANTIOXIDA? OR ANTI OXID?) AND ((MENTAL? OR NEUR?)(5A)(DEGENERAT ? OR DETERIORAT? OR CAPACIT?) OR NEURODEGENERAT? OR DEMENTIA)

=> s (l15 or l22) and (diet? or nutrit? or nutrien?) and (cat or feline or kitten or dog or canine or puppy)
L23 2 FILE MEDLINE
L24 1 FILE CAPLUS
L25 4 FILE BIOSIS
L26 2 FILE EMBASE
L27 0 FILE JICST-EPLUS
L28 2 FILE WPIDS

TOTAL FOR ALL FILES
L29 11 (L15 OR L22) AND (DIET? OR NUTRIT? OR NUTRIEN?) AND (CAT OR FELINE OR KITTEN OR DOG OR CANINE OR PUPPY)

=> dup rem l29
PROCESSING COMPLETED FOR L29
L30 10 DUP REM L29 (1 DUPLICATE REMOVED)

=> d cbib abs 1-10;s wedekind, k?/au,in

L30 ANSWER 1 OF 10 WPIDS (C) 2002 THOMSON DERWENT
AN 2002-105552 [14] WPIDS
CR 1998-557054 [47]; 2001-373633 [35]
AB US2001041741 A UPAB: 20020301
NOVELTY - **Nutritional** supplement comprises **L-carnitine**, Coenzyme Q10 (Ubiquinone) or their functional analogs and taurine or its precursor.
ACTIVITY - Cardiant; Anti-HIV; Cytostatic; Immunomodulator; Antibacterial; Immunosuppressive; Nephrotropic; Respiratory; Immunostimulant; Muscular.
MECHANISM OF ACTION - None given.
USE - For treating a disease, disorder or abnormal physical state consisting of heart disease and functional **deterioration** associated with ageing or increasing **neuromuscular** or athletic performance in mammals such as **dogs**, **cats** and preferably humans (claimed). Also useful in treatment of chronic degenerative disease, immune diseases such as AIDS, chronic multisystem disease, chronic lung or renal disease, chronic fatigue syndrome, patients on immunosuppressive drug post-transplantation, cancer patients on doxorubicin or related drugs, wasting or cachexia from cancer or sepsis.
ADVANTAGE - The composition potentiates the action of each component on cell function and energetics. The composition provides a more reliable and effective treatment to various diseases. The composition also corrects abnormalities in myocardial energetics, intracellular calcium and oxidative stress. The composition maintains and restores mitochondrial

function and prevents cardiac failure and aids recovery from cardiac disease.
Dwg.0/6

L30 ANSWER 2 OF 10 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
2001:472167 Document No.: PREV200100472167. The effects of experience and **antioxidants** on size discrimination learning in the **dog**.
Rick, J. T. (1); Ikeda-Douglas, C. J.; Murphey, H.; Muggenberg, B.; Zicker, S.; Milgram, N. W. (1). (1) Dept. of Psychology, University of Toronto, Toronto, ON USA. Society for Neuroscience Abstracts, (2001) Vol. 27, No. 1, pp. 280. print. Meeting Info.: 31st Annual Meeting of the Society for Neuroscience San Diego, California, USA November 10-15, 2001 ISSN: 0190-5295. Language: English. Summary Language: English.
AB Free radicals such as O- are byproducts of cellular metabolism and are thought to play a role in **neural degeneration** and age-related cognitive impairment. Using a variety of visual tasks, we have examined age-related deficits in a **canine** model of cognition. Previously, we found cognitive impairments in old **dogs** to be dependent on task difficulty and previous experience (Milgram et al., 1994, Behav. Neurosci. 108:57-68). In the present experiment, we studied the effects of environmental enrichment and an **antioxidant**-rich **diet** on the learning ability of aged beagles using a size discrimination reversal task (2 between- and 1 within-subjects factors). Using blocks differing only in size, animals were taught to approach one block over the other. On reaching the performance criterion, the reward contingency was reversed and the **dogs** were required to approach the previously unrewarded block. We found that there was a significant effect of **nutrition**, with animals on the enriched **diet** performing better than those on the control **diet**. The **dogs** in the control environment committed significantly more errors on the reversal, suggesting that enrichment improves an animal's ability to deal with changes in environmental contingencies.

L30 ANSWER 3 OF 10 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
2001:472166 Document No.: PREV200100472166. The effects of **diet** and age on the performance of the landmark discrimination learning task.
Estrada, J. (1); Ikeda-Douglas, C.; Milgram, N. W.; Zicker, S.. (1) Inst Med Sci, University of Toronto, Toronto, ON Canada. Society for Neuroscience Abstracts, (2001) Vol. 27, No. 1, pp. 279. print. Meeting Info.: 31st Annual Meeting of the Society for Neuroscience San Diego, California, USA November 10-15, 2001 ISSN: 0190-5295. Language: English. Summary Language: English.
AB Free radicals, which are byproducts of oxidative reactions, are an essential factor in the **degenerative neural** changes that accompany aging. We fed 19 old beagle **dogs** (10-14 years of age) a **diet** consisting of a broad spectrum of **antioxidants** and tested the effects on series of landmark discrimination problems(Land-0, 1 and 2). The task required the animals to respond selectively to the object closest to an external landmark. This task is particularly useful in identifying age-dependent cognitive impairment. The **dogs** were divided into 2 groups receiving control or an **antioxidant**-enriched **diet**. Animals on enriched **diet** learned the landmark task (Land-1) more rapidly than **dogs** on the control **diet**. These results show that performance in allocentric task can be improved by the administration of an **antioxidant** enriched **diet**.

L30 ANSWER 4 OF 10 MEDLINE DUPLICATE 1
2001541737 Document Number: 21473529. PubMed ID: 11588988. Assessment of **dietary** therapies in a **canine** model of Batten disease.
Siakotos A N; Hutchins G D; Farlow M R; Katz M L. (Department of Pathology, Indiana University School of Medicine, 635 Barnhill Drive,

Indianapolis, IN 46202, USA.. asiakoto@iupui.edu) . EUROPEAN JOURNAL OF PAEDIATRIC NEUROLOGY, (2001) 5 Suppl A 151-6. Journal code: DGS; 9715169. ISSN: 1090-3798. Pub. country: England: United Kingdom. Language: English.

AB The neuronal ceroid lipofuscinoses (NCLs) are inherited **neurodegenerative** diseases that occur in a number of animal species, including **dogs**. A study was conducted to determine whether the resupply of **nutrients** lost in NCL English Setter **dogs** would modify the course of the disease. Carnitine and polyunsaturated fatty acids have been reported to be reduced in NCL English Setters. Therefore, the normal laboratory **diets** of NCL **dogs** were supplemented with carnitine, fish oil and corn oil and the disease progression was compared with that of an untreated litter mate. The following specific prognostic indicators of NCL were monitored: cognitive function, brain atrophy, brain glucose metabolism and lifespan. Carnitine, with or without lipid supplements, dramatically delayed the progression of cognitive decline in NCL **dogs**. When fish oil and corn oil only were supplied, brain atrophy was reduced. A combination of all three supplements preserved cognitive function and increased lifespan by 10%. However, brain glucose hypometabolism and cerebral atrophy were not reduced. The results in this study indicated that the effectiveness of therapeutic interventions can be assessed by non-invasive methods at a relatively early stage of the disease process. Our study suggests that **dietary** supplementation with carnitine is a promising new approach for delaying or preventing the cognitive decline in **dogs**, and perhaps, with human NCL patients.

L30 ANSWER 5 OF 10 WPIDS (C) 2002 THOMSON DERWENT

AN 2000-514772 [46] WPIDS

AB WO 200044375 A UPAB: 20000921

NOVELTY - Method for increasing the plasma **vitamin E** level in a **cat** or **dog** comprises administration of sufficient **vitamin E**, optionally with also **vitamin C**, taurine, and/or a carotenoid; and a **dog** or **cat** foodstuff which delivers a sufficient concentration of ingredients to increase the **antioxidant** status of the animal.

DETAILED DESCRIPTION - Method for increasing the plasma **vitamin E** level in a **cat** or **dog**, by administration of sufficient **vitamin E**, optionally also with addition of **vitamin C** and/or taurine and/or a carotenoid, either simultaneously, separately, or sequentially, is new.

INDEPENDENT CLAIMS are included for:

(1) a **dog** or **cat** foodstuff which delivers a sufficient concentration of ingredients to increase the **antioxidant** status of the animal;

(2) use of **vitamin E** in the manufacture of a clinical **diet** for the prevention or treatment of any disorder which has a component of oxidative stress (sic; the previous limitation to **dogs** and **cats** is omitted); and

(3) a **dog** or **cat** food containing **vitamin C** at a 15 mg/400 kcal or above.

ACTIVITY - **Antioxidant**; Cytostatic; Cardiant; Antiarteriosclerotic; Antiarthritic; Ophthalmological; Antiinflammatory; Nephrotropic; Neuroprotective; Immunostimulant.

MECHANISM OF ACTION - None given.

USE - The **vitamin E** and/or C, optionally including also taurine and/or carotenoid, is of use in conditions resulting from oxidative stress, resulting in a healthier animal. These conditions include cancer, aging, heart disease, atherosclerosis, arthritis, cataracts, inflammatory bowel or renal disease, renal failure, **neurodegenerative** disease, or compromised immunity. The composition is also of value in treating or assisting the animal in

response to an immunological challenge, e.g. vaccination, optimizing and/or boosting the desired effect.

ADVANTAGE - **Vitamins E** and C are synergistic and complement each other, one being lipid-soluble and the other water-soluble.

Dwg.0/9

L30 ANSWER 6 OF 10 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.

2001:76899 Document No.: PREV200100076899. Landmark discrimination learning in aged **dogs** is improved by treatment with an **antioxidant** enriched **diet**. Milgram, N. W. (1); Estrada, J.; Ikeda-Douglas, C.; Castillo, J.; Head, E.; Cotman, C. W.; Murphey, H.; Holowachuk, D.; Muggenburg, B.; Zicker, S.. (1) Univ Toronto, Toronto, ON Canada. Society for Neuroscience Abstracts, (2000) Vol. 26, No. 1-2, pp. Abstract No.-193.9. print. Meeting Info.: 30th Annual Meeting of the Society of Neuroscience New Orleans, LA, USA November 04-09, 2000 Society for Neuroscience. ISSN: 0190-5295. Language: English. Summary Language: English.

AB Reactive oxygen species, which are byproducts of cellular metabolism, are potentially critically important contributors to **degenerative neural** changes that accompany aging. We fed a **canine diet** consisting of a broad spectrum of **antioxidants** and tested the effects on age-dependent cognitive deterioration in beagle **dogs**. Young and aged beagle **dogs** were each divided into groups receiving either control or **antioxidant**-enriched **diets**. The **dogs** were placed on the **diet** for either 0 or 5 weeks, and were then tested on a series of discrimination problems, all of which required the animals to respond selectively to the object closest to an external landmark. The aged animals on the enriched **diet** learned all of the tasks more rapidly than did the aged animals on the control **diet**. More consistent improvement was seen initially in the animals given 5 weeks of **diet** before testing. The young animals, by contrast, showed no effect of **diet** . These results both further support a free radical model of age-dependent **neurodegeneration** and indicate that short-term administration of **antioxidants** can partially reverse the deleterious effects of aging on cognition.

L30 ANSWER 7 OF 10 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.

2000:8982 Document No.: PREV200000008982. Multiple **antioxidants** in the prevention and treatment of Parkinson's disease. Prasad, Kedar N. (1); Cole, William C.; Kumar, Bipin. (1) UCHSC, 4200 E. 9th Ave., Denver, CO, 80262 USA. Journal of the American College of Nutrition, (Oct., 1999) Vol. 18, No. 5, pp. 413-423. ISSN: 0731-5724. Language: English. Summary Language: English.

AB Parkinson's disease (PD) is one of the major progressive neurological disorders for which no preventative or long-term effective treatment strategies are available. Epidemiologic studies have failed to identify specific environmental, **dietary** or lifestyle risk factors for PD except for toxic exposure to manganese, meperidine (Demerol(R), the "designer drug" version of which often contains a toxic byproduct of the synthesis, 1-methyl-4-phenyl 1,2,3,6 tetrahydropyridine (MPTP)), and some herbicides and pesticides. The search for genetic risk factors such as mutation, overexpression or underexpression of nuclear genes in DA neurons in idiopathic PD has not been successful as yet. Polymorphism in certain genes appears to be a risk factor, but there is no direct evidence for the causal relationship between polymorphism and increased risk of PD. In familial PD, mutation in the alpha-synuclein gene is associated with the disease, but a direct role of this gene in **degeneration** of DA **neurons** remains to be established. Although mutations in the Parkin gene has been associated with autosomal recessive juvenile Parkinson's disease, the role of this gene mutation in causing

**degeneration** of DA **neurons** has not been defined. We have reported that in hereditary PD, a mutation in the alpha-synuclein gene may increase the sensitivity of DA neurons to neurotoxins. We hypothesize that, in idiopathic PD, epigenetic (mitochondria, membranes, protein modifications) rather than genetic events are primary targets winch, when impaired, initiate **degeneration** in DA **neurons**, eventually leading to cell death. Although the nature of **neurotoxins** that cause **degeneration** in DA **neurons** in PD is not well understood, oxidative stress is one of the intermediary risk factors that could initiate and/or promote **degeneration** of DA **neurons**. Therefore, supplementation with **antioxidants** may prevent or reduce the rate of progression of this disease. Supplementation with multiple **antioxidants** at appropriate doses is essential because various types of free radicals are produced, **antioxidants** vary in their ability to quench different free radicals and cellular environments vary with respect to their lipid and aqueous phases. L-dihydroxyphenylalanine (L-dopa) is one of the agents used in the treatment of PD. Since L-dopa is known to produce free radicals during its normal metabolism, the combination of L-dopa with high levels of multiple **antioxidants** may improve the efficacy of L-dopa therapy.

L30 ANSWER 8 OF 10 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.

93311433 EMBASE Document No.: 1993311433. Neuroprotective actions of glucocorticoid and nonglucocorticoid steroids in acute neuronal injury. Hall E.D.. Central Nervous System Diseases Res., Upjohn Company,Kalamazoo, MI 49001, United States. Cellular and Molecular Neurobiology 13/4 (415-432) 1993.
ISSN: 0272-4340. CODEN: CMNEDI. Pub. Country: United States. Language: English. Summary Language: English.

AB 1. The glucocorticoid steroid methylprednisolone (MP) has been shown to enhance chronic recovery after human spinal cord injury when administered in a 24-hr high-dose regimen beginning within 8 hr. The doses of MP that affect this improved recovery have been demonstrated to inhibit posttraumatic spinal cord lipid peroxidation (LP), which has been postulated to be a key event in the secondary injury-induced degenerative cascade. 2. The molecular mechanism of action of the steroid appears to involve intercalation into the cell membrane and blockade of the propagation of peroxidative reactions. At a physiological level, the inhibition of injury-induced LP has been found to result in an attenuation of progressive posttraumatic ischemia and energy failure together with an augmented reversal of intracellular calcium accumulation. However, MP also acts directly to retard secondary **neuronal degeneration** as observed in studies showing the steroid's ability to slow the anterograde degeneration of experimentally injured **cat** soleus motor nerves. 3. The duplication of this effect by the nonsteroidal lipid **antioxidant** .alpha.- tocopherol supports the notion that is indeed a manifestation of the inhibition of posttraumatic LP. Moreover, the efficacy of MP in limiting lipid peroxidation and secondary spinal cord or motor nerve degeneration has also been duplicated by a nonglucocorticoid 21-aminosteroid tirilazad mesylate (U-74006F), which suggests the independence of the **antioxidant** and glucocorticoid effects of MP.

L30 ANSWER 9 OF 10 MEDLINE

90133985 Document Number: 90133985. PubMed ID: 2614850. Mechanisms of **neuronal degeneration** secondary to central nervous system trauma or ischemia. Hall E D; Yonkers P A. JOURNAL OF NEUROTRAUMA, (1989 Winter) 6 (4) 227-8. Journal code: J82; 8811626. ISSN: 0897-7151. Pub. country: United States. Language: English.

L30 ANSWER 10 OF 10 CAPLUS COPYRIGHT 2002 ACS

Searched by: Mary Hale 308-4258 CM-1 12D16

1970:10426 Document No. 72:10426 **Vitamin E** deficiency and fat stress in the **dog**. Hayes, K. C.; Nielsen, S. W.; Rousseau, J. E., Jr. (Univ. of Connecticut, Storrs, Conn., USA). J. Nutr., 99(2), 196-209 (English) 1969. CODEN: JONUAI.

AB Thirty-two male beagle **puppies** were fed **vitamin E**-deficient **diets** with 4 levels (1, 5, 10, and 15%) of safflower oil with or without a **vitamin E** supplement for a 15-week period. The unsupplemented **dogs** developed a **vitamin E** deficiency which was correlated with increased dialuric acid hemolysis of red cells and decreased plasma tocopherol values. Both Hb and packed cell vol. were depressed by increasing fat consumption, unrelated to tocopherol supplementation and attributed to in vivo red cell disruption. Creatine phosphokinase values were elevated in tocopherol-deficient **dogs** and were correlated with fat consumption. Terminal plasma vitamin A concns. were lower in **dogs** receiving <1% supplementary fat. At necropsy, browning of the intestinal muscularis in the tocopherol-deficient **dogs** was related to the consumption of polyunsatd. fats (PUFA). Microscopically, lipofuscin was seen in smooth muscle of gut, urinary bladder, and small arterioles. **Neuroaxonal** dystrophy and myo-**degeneration** were also found in the **vitamin E**-deficient **dogs**. The requirement for tocopherol was directly related to PUFA consumption, apparently assocd. with the metabolism of the fat and not with an **antioxidant** role of the vitamin.

```
'IN' IS NOT A VALID FIELD CODE
L31          18 FILE MEDLINE
L32          20 FILE CAPLUS
L33          38 FILE BIOSIS
'IN' IS NOT A VALID FIELD CODE
L34           7 FILE EMBASE
L35           0 FILE JICST-EPLUS
L36           3 FILE WPIDS

TOTAL FOR ALL FILES
L37          86 WEDEKIND, K?/AU,IN

=> s zicker, s?/au,in
'IN' IS NOT A VALID FIELD CODE
L38          15 FILE MEDLINE
L39           9 FILE CAPLUS
L40          20 FILE BIOSIS
'IN' IS NOT A VALID FIELD CODE
L41           4 FILE EMBASE
L42           0 FILE JICST-EPLUS
L43           1 FILE WPIDS

TOTAL FOR ALL FILES
L44          49 ZICKER, S?/AU,IN

=> s 137 and 144
L45           0 FILE MEDLINE
L46           0 FILE CAPLUS
L47           0 FILE BIOSIS
L48           0 FILE EMBASE
L49           0 FILE JICST-EPLUS
L50           0 FILE WPIDS

TOTAL FOR ALL FILES
L51           0 L37 AND L44
```

Searched by: Mary Hale 308-4258 CM-1 12D16

=> s (137 or 144)
L52 33 FILE MEDLINE
L53 29 FILE CAPLUS
L54 58 FILE BIOSIS
L55 11 FILE EMBASE
L56 0 FILE JICST-EPLUS
L57 4 FILE WPIDS

TOTAL FOR ALL FILES
L58 135 (L37 OR L44)

=> s l58 and ((mental? or neur?)(5a)(degenerat? or deteriorat? or capacit?) or neurodegenerat? or neuro degenerat? or dementia? or mental?)
L59 0 FILE MEDLINE
L60 0 FILE CAPLUS
L61 3 FILE BIOSIS
L62 0 FILE EMBASE
L63 0 FILE JICST-EPLUS
L64 0 FILE WPIDS

TOTAL FOR ALL FILES
L65 3 L58 AND ((MENTAL? OR NEUR?)(5A)(DEGENERAT? OR DETERIORAT? OR CAPACIT?) OR NEURODEGENERAT? OR NEURO DEGENERAT? OR DEMENTIA? OR MENTAL?)

=> d 1-3 cbib abs

L65 ANSWER 1 OF 3 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
2001:472167 Document No.: PREV200100472167. The effects of experience and antioxidants on size discrimination learning in the dog. Rick, J. T. (1); Ikeda-Douglas, C. J.; Murphey, H.; Muggenberg, B.; **Zicker, S.**; Milgram, N. W. (1). (1) Dept. of Psychology, University of Toronto, Toronto, ON USA. Society for Neuroscience Abstracts, (2001) Vol. 27, No. 1, pp. 280. print. Meeting Info.: 31st Annual Meeting of the Society for Neuroscience San Diego, California, USA November 10-15, 2001 ISSN: 0190-5295. Language: English. Summary Language: English.

AB Free radicals such as O- are byproducts of cellular metabolism and are thought to play a role in **neural degeneration** and age-related cognitive impairment. Using a variety of visual tasks, we have examined age-related deficits in a canine model of cognition. Previously, we found cognitive impairments in old dogs to be dependent on task difficulty and previous experience (Milgram et al., 1994, Behav. Neurosci. 108:57-68). In the present experiment, we studied the effects of environmental enrichment and an antioxidant-rich diet on the learning ability of aged beagles using a size discrimination reversal task (2 between- and 1 within-subjects factors). Using blocks differing only in size, animals were taught to approach one block over the other. On reaching the performance criterion, the reward contingency was reversed and the dogs were required to approach the previously unrewarded block. We found that there was a significant effect of nutrition, with animals on the enriched diet performing better than those on the control diet. The dogs in the control environment committed significantly more errors on the reversal, suggesting that enrichment improves an animal's ability to deal with changes in environmental contingencies.

L65 ANSWER 2 OF 3 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
2001:472166 Document No.: PREV200100472166. The effects of diet and age on the performance of the landmark discrimination learning task. Estrada, J. (1); Ikeda-Douglas, C.; Milgram, N. W.; **Zicker, S.**. (1) Inst Med Sci, University of Toronto, Toronto, ON Canada. Society for Neuroscience Abstracts, (2001) Vol. 27, No. 1, pp. 279. print. Meeting Info.: 31st

Searched by: Mary Hale 308-4258 CM-1 12D16

Annual Meeting of the Society for Neuroscience San Diego, California, USA November 10-15, 2001 ISSN: 0190-5295. Language: English. Summary Language: English.

AB Free radicals, which are byproducts of oxidative reactions, are an essential factor in the **degenerative neural** changes that accompany aging. We fed 19 old beagle dogs (10-14 years of age) a diet consisting of a broad spectrum of antioxidants and tested the effects on series of landmark discrimination problems(Land-0, 1 and 2). The task required the animals to respond selectively to the object closest to an external landmark. This task is particularly useful in identifying age-dependent cognitive impairment. The dogs were divided into 2 groups receiving control or an antioxidant-enriched diet. Animals on enriched diet learned the landmark task (Land-1) more rapidly than dogs on the control diet. These results show that performance in allocentric task can be improved by the administration of an antioxidant enriched diet.

L65 ANSWER 3 OF 3 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.

2001:76899 Document No.: PREV200100076899. Landmark discrimination learning in aged dogs is improved by treatment with an antioxidant enriched diet. Milgram, N. W. (1); Estrada, J.; Ikeda-Douglas, C.; Castillo, J.; Head, E.; Cotman, C. W.; Murphey, H.; Holowachuk, D.; Muggenburg, B.; **Zicker, S.**. (1) Univ Toronto, Toronto, ON Canada. Society for Neuroscience Abstracts, (2000) Vol. 26, No. 1-2, pp. Abstract No.-193.9. print. Meeting Info.: 30th Annual Meeting of the Society of Neuroscience New Orleans, LA, USA November 04-09, 2000 Society for Neuroscience. ISSN: 0190-5295. Language: English. Summary Language: English.

AB Reactive oxygen species, which are byproducts of cellular metabolism, are potentially critically important contributors to **degenerative neural** changes that accompany aging. We fed a canine diet consisting of a broad spectrum of antioxidants and tested the effects on age-dependent cognitive deterioration in beagle dogs. Young and aged beagle dogs were each divided into groups receiving either control or antioxidant-enriched diets. The dogs were placed on the diet for either 0 or 5 weeks, and were then tested on a series of discrimination problems, all of which required the animals to respond selectively to the object closest to an external landmark. The aged animals on the enriched diet learned all of the tasks more rapidly than did the aged animals on the control diet. More consistent improvement was seen initially in the animals given 5 weeks of diet before testing. The young animals, by contrast, showed no effect of diet. These results both further support a free radical model of age-dependent **neurodegeneration** and indicate that short-term administration of antioxidants can partially reverse the deleterious effects of aging on cognition.

=> del his y

=> fil casrea

| COST IN U.S. DOLLARS | SINCE FILE ENTRY | TOTAL SESSION |
|---|---|---|
| FULL ESTIMATED COST | 124.16 | 402.45 |

| DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS) | SINCE FILE ENTRY | TOTAL SESSION |
|---|---|---|
| CA SUBSCRIBER PRICE | -0.62 | -1.86 |

FILE 'CASREACT' ENTERED AT 15:39:29 ON 02 MAY 2002


Searched by: Mary Hale 308-4258 CM-1 12D16